REMARKS

Claims 1-5 and 17-30 are pending. Claims 1, 4 and 5 are amended. Claims 9-16 are withdrawn from consideration. Basis for the amendments can be found in the application and claims as originally filed. No new matter is added.

Claim Rejections under 35 U.S.C. §112, first paragraph: Lack of Enablement

Claims 1-5 and 17-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain disorders of amyloidosis, allegedly does not reasonably provide enablement for all disorders of amyloidosis. The Office Action alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicant respectfully requests reconsideration of the rejection in view of the amendments and arguments herein.

Relevant Law

To satisfy the enablement requirement of 35 U.S.C §112, first paragraph, the specification must teach one of skill in the art to make and use the invention without undue experimentation. *Atlas Powder Co. v. E.I. DuPont de Nemours*, 750 F.2d 1569, 224 USPQ 409 (1984).. This requirement can be met by providing sufficient disclosure, either through illustrative examples or terminology, to teach one of skill in the art how to make and how to use the claimed subject matter without undue experimentation. This clause does not require "a specific example of everything *within the scope* of a broad claim." *In re Anderson*, 176 USPQ 331, at 333 (CCPA 1973), emphasis in original. Rather, the requirements of §112, first paragraph "can be fulfilled by the use of illustrative examples or by broad terminology." *In re Marzocci et al.*, 469 USPQ 367 (CCPA 1971)(emphasis added).

The inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the claimed invention. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or

guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

PTO Guidelines

In determining whether any experimentation is "undue," the above-noted factors are to be considered. As instructed in the published PTO guidelines and in accord with the case law noted above, it is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The analysis must consider all the evidence related to each of the factors, and any conclusion of non-enablement must be based on the evidence as a whole. *Id.* 8 USPQ2d at 1404 & 1407.

The starting point in an evaluation of whether the enablement requirement is satisfied is an analysis of each claim to determine its scope. As set forth in the guidelines, all questions of enablement are evaluated against the claimed subject matter. The focus of the inquiry is whether everything within the scope of the claim is enabled. With respect to scope of enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971). Once the scope of the claims is addressed, a determination must be made as to whether one skilled in the art is enabled to make and use the entire scope of the claimed invention without undue experimentation.

Analysis

Applying the above factors to the instant claims, applicant respectfully submits that as described in detail below, it would not require undue experimentation to practice the instantly claimed subject matter.

Scope of the claims

Claim 1 is directed to a method of treating amyloidosis associated with Alzheimer's disease and islet amyloid fibrils, in a mammal suffering therefrom by administration to the

mammal of a therapeutically effective amount of a compound described therein. Claims 2-5 and 17-30 depend from claim 1 and further define the method and the compounds used therein.

The level of skill in the art is high

The level of skill in this art is recognized to be high (see, e.g., Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986)). In addition, the numerous articles and patents that are of record in this application that are authored by those of a high level of skill for an audience of a high level of skill further evidences the high level of skill in this art.

The amount of direction and guidance presented, teachings in the specification

As described herein, the claims are directed a method of treating amyloidosis associated with Alzheimer's disease and islet amyloid fibrils, in a mammal suffering therefrom by administration to the mammal a therapeutically effective amount of a compound described therein. The specification describes on page 16, lines 15-20, that compounds of the instantly claimed methods act to inhibit or prevent amyloid fibril formation, inhibit or prevent amyloid fibril growth, and/or cause disassembly, disruption, and/or disaggregation of preformed amyloid fibrils and amyloid protein deposits. The *in vitro* methods to measure the activity these compounds in amyloidosis associated with Alzheimer's disease are described in Examples 1 through 4, on pages 21-26 and Assay 1, on page 28. The specification on pages 28-29, also describes an *in vivo* assay (assay 2) to measure the activity of the compounds of instantly claimed methods and drug products against conditions associated with amyloidoses, such as Alzheimer's disease in humans. The exemplary embodiments described in the specification demonstrate disassembly/disruption of Alzheimer's disease Aβ 1-42 fibrils, dose-dependent disassembly/disruption of Alzheimer's disease Aβ 1-40 fibrils, disaggregation of Alzheimer's disease Aβ 1-40 fibrils, dose-dependent disaggregation of Alzheimer's disease Aβ 1-40 fibrils and disassembly/disruption of islet amyloid fibrils (amylin) by several compounds within the scope of instant claims. The specification also discloses that further *in vitro* and *in vivo* assays may be used to test the compounds for their effectiveness in the treatment of Alzheimer's disease, such as those described in European Published Patent Application No. 0 659 418.

Therefore, the application provides sufficient guidance for one of skill in the art to make and use the full scope of the instantly claimed subject matter.

Knowledge of those of skill in the art

At the time of the effective filing date of this application and before, the skilled artisan knew conditions associated with amyloid protein deposition including Alzheimer's disease and conditions associated with deposition and accumulation of islets amyloid fibrils. Amyloidosis and various conditions associated with it are described in a large volume of literature.

A Guide to Understanding Alzheimer's Disease and Related Disorders, Jorm, ed., New York University Press, New York, 1987, describes association of amyloidosis with Alzheimer's Disease.

U.S. Patent 5,981,168 describes amyloidoses of the central nervous system include, for example, Alzheimer's disease.

U.S. patent 5,869,469 describes amyloidosis as a pathological condition characterized by, for example Alzheimer's disease, and systemic or localized diseases such as adult-onset diabetes.

U.S. patent 5,972,956 also describes amyloidosis and diseases associated, including Alzheimer's disease.

Therefore, at the time of the effective filing date of this application and before, the skilled artisan was well- aware of amyloidosis associated with Alzheimer's disease and islet amyloid fibrils. There is a large body of literature directed to the description of the amyloidosis associated with Alzheimer's disease and islet amyloid fibrils.

Presence of working examples

The application provides working examples to demonstrate the instantly claimed methods of treating amyloidosis associated with Alzheimer's disease and islet amyloid fibrils. The application provides working examples where the instantly claimed method is demonstrated for the treatment of exemplary conditions associated with amyloidosis, such as Alzheimer's disease and type II diabetes. Working examples 1-4 in the specification illustrate disassembly/disruption of Alzheimer's disease Aβ 1-42 fibrils by the compounds used in the instantly-claimed methods and drug products, dose-dependent disassembly/disruption of Alzheimer's disease Aβ 1-40

fibrils by tannic acid and gallic acid which are within the scope of the compounds used in the instant claims, disaggregation of Alzheimer's disease Aβ 1-40 fibrils by the compounds used in the instantly-claimed methods and drug products, dose-dependent disaggregation of Alzheimer's disease Aβ 1-40 fibrils by tannic acid and gallic acid which are within the scope of the compounds used in the instant claims. The specification demonstrates the application of instantly claimed methods for disassembly/disruption of islet amyloid fibrils in treating type II diabetes in example 5. Further, the specification also provides *in vitro* and *in vivo* assays to test the compounds for their effectiveness in the treatment of Alzheimer's disease.

Conclusion

As discussed above, the instant specification describes and exemplifies amyloidosis associated with Alzheimer's disease and islet amyloid fibrils. There is vast quantity of literature describing amyloidosis associated with Alzheimer's disease and islet amyloid fibrils. The working examples in the specification demonstrate disassembly/disruption of Alzheimer's disease Aβ 1-42 fibrils, dose-dependent disassembly/disruption of Alzheimer's disease Ab 1-40 fibrils, disaggregation of Alzheimer's disease Aβ 1-40 fibrils, dose-dependent disaggregation of Alzheimer's disease Aβ 1-40 fibrils and disassembly/disruption of islet amyloid fibrils (amylin) by several compounds within the scope of the instant claims. Therefore, in light of the scope of the claims, the description and the working examples in the application, the high level of skill of those in this art, and the extensive knowledge of those of skill in this art, it would not require undue experimentation to practice full scope of the claims. Applicant respectfully requests reconsideration and removal of the rejection.

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Attorney's Docket No.: 17170-002001

In view of the above, examination of the application on the merits and allowance is respectfully requested.

There is no fee required to file this Amendment in the above application. However, if any fees do apply, please charge them to, or apply any credits to Deposit Account 06-1050.

Respectfully submitted,

Date: 10/8/04

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